ARTIGO DE REVISÃO

RELATIONSHIP BETWEEN CHRONOBIOLOGY AND AGING: ADJUSTMENTS FACING THE TECHNOLOGICAL WORLD

A relação entre cronobiologia e o envelhecimento: adaptações diante do mundo tecnológico

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ABSTRACT

Although there is no consensus in literature regarding which are the rhythmicity changes that occur during the aging process, it is believed that advanced age may affect the circadian rhythms, leading to a decreased ability to tolerate abrupt phase shift, decreased amplitude of rhythms, phase advance and reduced endogenous period. Therefore, understanding the mechanisms involved in the aging process has become essential for the development of new treatment approaches in order to improve quality of life of the elderly population. The use of technologies has increased over the past years, becoming an important factor to be considered an influence in the circadian rhythms. There is a limited number of studies linking the relationship between sleep-wake cycle and the effect of light and media use in the modern world. Thus, the aim of this review was to analyze the relationship between light, technology, and circadian rhythms in the elderly population.

KEYWORDS: circadian rhythm; sleep; aging; aged.

RESUMO

Apesar de não haver consenso na literatura no que diz respeito às mudanças na ritmicidade que ocorrem durante o envelhecimento, acredita-se que a idade avançada possa afetar os ritmos circadianos, levando a uma habilidade reduzida de tolerar mudanças abruptas de fase, redução da amplitude de ritmos, avanço de fase e redução do período endógeno. Consequentemente, o entendimento dos mecanismos envolvidos no processo de envelhecimento se tornou essencial para o desenvolvimento de novas abordagens terapêuticas com o objetivo de melhorar a qualidade de vida da população idosa. O uso de tecnologias vem aumentando ao longo dos últimos anos, se tornando um importante fator a ser considerado como influência para os ritmos circadianos. Há um número limitado de estudos relacionando o ciclo vigília/sono com os efeitos da luz e do uso de mídias no mundo moderno. Desta forma, o objetivo da presente revisão foi analisar a relação entre luz, tecnologia e ritmos circadianos na população idosa.

PALAVRAS-CHAVE: ritmo circadiano; sono; envelhecimento; idoso.

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INTRODUCTION

According to the Department of Human Rights, the elderly population in Brazil corresponded to 12% in 2011, and this number is expected to increase in the coming years. The aging of a population reflects an improvement in living conditions and explains the emergence of new needs. In response to social demands, understanding the mechanisms involved in the aging process and proposing actions that promote inclusion and independence of the elderly becomes essential. It is known that advanced age may have influence in the circadian rhythms; thus, the aim of this review was to analyze the relationship between light, technology and circadian rhythms in the elderly population.

Circadian rhythms are the product of the interaction between endogenous biological clocks and changes between day and night. The circadian system is synchronized by environmental cues, a process called entrainment. A rhythm is considered to be entrained when it maintains a steady relationship with the synchronizer agent. In the absence of external environmental cues, the clocks express their own endogenous period (lasting approximately 24h). The existence of a biological clock able to keep pace in the absence of environmental cues, a situation called free-running, ensures the proper functioning of the internal temporal relationships even in constant conditions.

The endogenous period observed in free-running conditions is set by molecular clocks, which have feedback loops lasting approximately — but not exactly — 24 hours. Individual variations on the duration of these loops may reflect in different endogenous periods and chronotypes (morning, intermediate and evening-types). A person’s chronotype results from the phase relationship between endogenous rhythms and light/dark cycle and expresses differences in the preference for a particular sleep schedule and a set time for activities. Thus, the morning chronotype show shorter endogenous period than the evening-type, and these differences may be associated with the speed of the molecular clock feedback loops. Morning-type subjects have earlier sleep onset and offset when compared to intermediate and evening-type, less variable duration of sleep episodes than the evening-types, and they also show phase advancement, with an earlier peak of body temperature, nocturnal melatonin secretion and morning peak of cortisol.

CIRCADIAN RHYTHMS IN ELDERLY

It is known that the circadian system undergoes changes throughout its development, especially in early and late stages of life, and different biological rhythms have been studied as markers of what and how these changes occur. In early life, the changes are related to the maturation of the endogenous system and its adaptation to the environment. Although there is no consensus, most studies reporting changes in old age focus on decreased ability to tolerate abrupt phase shift (i.e. jetlag), decreased amplitude of rhythms, phase advance and reduced endogenous period. However, most of them are between-subjects studies, in which elderly people are compared to different young subjects. This issue is well addressed in a review by Myers & Badia, where they argue that it may result in a biased sample of elderly subjects, since not all seniors have the same opportunity to be sampled due to the high mortality rate in this group when compared to young subjects, leading to a non-representative sample of elderly subjects (e.g. selected subjects are relatively healthier, which may be associated with a good maintenance of the circadian rhythm and sleep quality).

Therefore, many of the reported changes, or the lack of these changes, may be mere artifacts. Thus, it is worth emphasizing the importance of longitudinal within-subject studies to better understand the changes in circadian rhythms in elderly people. This discussion could explain the large number of conflicting studies in the area. However, although there is no consensus, literature provides enough information to speculate on the matter, especially regarding the mechanisms which could lead to such changes on the circadian system in aging.

Despite most studies with animal models demonstrating phase shift adaptations in older individuals, few studies have evaluated this phenomenon in elderly people. Regarding the effects of jetlag on pilots of different ages, there is evidence of sleep deficits caused by changes in time zones, whose effects can be up to 3.5 times worse in older pilots. Evaluating older night-shift workers by questionnaires, it was observed that they show more distress to synchronize their endogenous rhythms than young workers, especially the sleep-wake cycle. After three nights of night shift, it was also shown that older workers present greater deficits in their ability to recover the temperature rhythm when compared to young adults, although this difference has not been observed when assessed after only one night shift. However, there are studies that contradict these findings, indicating that despite the fact that there are changes in melatonin rhythm and temperature amplitude, and that fragmentation of sleep exists, there is no difference in the phase adjustment between young and elderly subjects. Assessing the methodology used in the studies previously mentioned, we can see that their results
point out to differences in the adaptation to phase shifts between young and older people using subjective methods such as questionnaires. On the other hand, studies that used objective measures (i.e. plasmatic melatonin concentration and body temperature) did not observe these differences between ages. Therefore, the impaired ability to adapt to phase shifts, as seen in the elderly sample relative to sleep complaints, is based on subjective reports; however, these findings are not supported by the corresponding laboratory data.

The most discussed explanation referring to the lower capability of adjustment to abrupt phase shifts seen in the elderly population, as proposed by Andlauer et al., is based on the fact that they present a reduction in circadian rhythms amplitude. This reduction would lead to impairment in the temporal signaling, leading to an inability of synchronizing the system in response to a phase shift. Therefore, according to this hypothesis, a greater amplitude of synchronizing the system in response to a phase shift.

Regarding the body core temperature rhythms in elderly subjects, data suggests reduction of the amplitude when compared to young adults, and similar reduction can be found concerning other rhythms, such as cortisol secretion and alertness. It is speculated that these changes in the amplitude may be the results of alterations of the neural and chemical signals magnitude, which are dependent of the sleep-wake cycle; these signals being the ones sent to or produced by the suprachiasmatic nuclei (SCN). The attenuation of these signals may occur for various ontogenetic factors, as the reduction of retinal sensitivity to light, morphological, chemical and genetic expression changes in the SCN, and changes in the pineal gland. A reduction of the retinal sensitivity is also associated to behavioral changes inherent to the aging process, especially via reduction of bright light exposure. These two factors combined are able to significantly exacerbate the temporal signaling impairments, resulting in damped rhythms and signals, which are incapable of entraining the circadian rhythm.

The phase advance observed in the elderly population may be found in many different rhythms: elderly people present earlier sleep onset and sleep offset when compared to young adults, earlier nadir of the body temperature, and advanced acrophase of the rest-activity rhythm. This advance of phase is commonly explained by another change in the aging of the circadian system: the shortening of the endogenous period (\( \tau \)). As the endogenous period of elderly people is usually shorter than 24 hours, the cycle is completed more rapidly, leading to an earlier phase day after day. However, as will be discussed further, studies addressing the shortening of \( \tau \) throughout the aging process are conflicting; hence, this change is not well sustained by the literature. Moreover, a study conducted by Duffy et al. showed that the habitual sleep time for elderly subjects differs from the melatonin rhythm, which also presents an advanced phase, i.e. the elderly subjects are not just waking up earlier but are also advanced with respect to their own melatonin rhythm.

This observation suggests that if the \( \tau \) shortening actually exists, the advance in the sleep/wake cycle in elderly people cannot be explained by these changes in endogenous period.

As previously mentioned, studies evaluating aging and endogenous period are contradictory. Most studies showing \( \tau \) shortening were performed using animal models, and only a few of them were conducted with humans. Weitzman et al., studying young and elderly people under normal routine and subjected to free-running protocols, showed a shortening of endogenous period of the temperature rhythm, supporting the results obtained with animal models. However, there are consistent evidences suggesting that \( \tau \) does not change during aging. By using forced desynchronization protocols, no difference was found between young and elderly temperature rhythms. Paradoxically, a longitudinal study evaluating the secretion of melatonin in blind elderly people — which are continuously free-running — found a longer endogenous period. This fact counteracts the conventional explanation that the phase advance seen in the elderly population is due to shortened endogenous period.

An example of rhythm with well-established changes due to aging is the sleep/wake cycle. Newborns show a polyphasic pattern (sleep episodes occurring multiple times
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in a 24-hour period), but throughout the development until the end of adulthood this pattern becomes monophasic (only one episode of sleep in a 24-hour period). Elderly subjects usually present patterns that are similar to the polyphasic one, with the occurrence of naps as a common habit during the day in this population.

Another important change is the prevalence of certain chronotype related to age group. The characteristic phase delay of adolescents (who show delayed sleep onset) occurs early in puberty due to the association between physiological and social changes, which leads this population to be predominantly of evening-type. During the subsequent development, the sleep/wake cycle rhythm regresses to its original state and remains stable until about 35 years of age; after this point it begins to advance its phase (presenting earlier sleep onset) and leading to a tendency towards morningness in elderly people.32 Studies evaluating the ontogenesis of chronotype should take into account that gender differences exist, since men present greater plasticity in relation to their phenotype, then expressing greater range of changes during aging. Thus, the characteristic phase delay presented by adolescents and the phase advance presented by elderly subjects may be a highly associated phenomenon for males.33

CIRCADIAN RHYTHMS AND AGING DISEASES

Several factors may influence the sleep/wake cycle, including neurological/psychiatric disorders and the aging process. Evidences from postmortem studies have associated later life circadian disfunctioning with neuropathological findings and neurodegenerative diseases; however, these changes are not equal across different types of dementias.34,35

Sleep disturbances affect more than 80% of people over 65 years old,27 and among pathological patients this number can be even higher.26 Alterations in circadian function, as was previously described, can be exacerbated in Alzheimer’s disease (AD), with increased sleep/wake cycle rhythm fragmentation, nocturnal awakenings36 and daytime sleepiness,37 and may be more accentuated in institutionalized AD patients.38 These alterations may increase the risk of cognitive impairment (i.e. memory, attention, etc.).39 Although the alterations in circadian function appear to be associated with dementia, there are evidences suggesting that these changes may act as predictors for subsequent AD development, proposing that compromised rhythms might be a preclinical phenomenon.40 Considering the evidence of circadian dysfunction in AD, it becomes important to use therapeutic approaches that may improve these conditions, such as melatonin and light therapy interventions. There are studies showing rhythms stabilization and improved sleep quality after evening light exposure,41 improved scores on tasks evaluating mental state42 and delayed sleep onset after a period of morning light exposure.43

Regarding the circadian changes that happen in Parkinson’s disease (PD), sleep disturbances are one of the most common complications in addition to the motor impairment.44 It has been reported that 60 to 98% of PD patients present intense sleep fragmentation and excessive daytime sleepiness in comparison with healthy elderly controls.45,46 Besides, around 25 to 50% of patients with PD present rapid eye movement (REM) sleep behavior disorder or REM sleep without atonia. It has been proposed that REM sleep disorders may precede the onset of clinical symptoms of Parkinsonism, occurring many years earlier than PD itself. Based on that, most studies suggest that more extensive pathological changes in PD may involve brainstem areas related with the control of REM sleep and that those changes start very early in life.44

The main discussion of this topic refers to the fact that the circadian system shows considerable changes when affected by some kinds of diseases related to elderly people, such as AD and PD. As already mentioned, those changes can be summarized as an increase in sleep fragmentation and nocturnal awakenings, and excessive daytime sleepiness. A large body of studies suggests that these alterations in circadian rhythms could be considered preclinical symptoms (prodromes) and, therefore, could be used as a way to anticipate diagnoses, mainly regarding AD. However, the problem with this approach is that most of the changes can also be found in normal healthy aging patients, becoming extremely difficult to establish a limit of normality for the circadian rhythms alterations. In other words, we can rarely state with certainty if one alteration or another is pathological, because most of the changes could be considered regular characteristics of the aging brain.

CHRONOBIOLOGY, AGING AND THE MODERN WORLD

Exposure to light can affect the circadian clock in different ways, i.e., exposure to bright light from the end of the night period to early morning may lead the system to respond with a phase advance, whereas light exposure from late afternoon to evening results in a phase delay of its
rhythms. Considering the effects of light exposure, there are a few studies demonstrating the impacts of electric light on circadian rhythms, especially on sleep patterns. A study performed with adolescents showed that those without electric lighting at home present earlier sleep onset when compared to those who have access to artificial light. In agreement with this study, Pereira et al. showed that adolescents without electric lighting at home have longer sleep duration than those with electric lighting.

Wright et al. compared sleep parameters of young adults in two different moments — regular daily routine and one week of outdoor camping (no electric light exposure) — and demonstrated that parameters such as sleep onset and sleep offset, melatonin onset, midpoint and offset occurred approximately 2 h earlier during the camping period when compared to the week of habitual electric lighting exposure. A similar result was found by Moreno et al., which showed that rubber tappers of a population living/working in Amazon (stable natural light-dark cycle: ~ LD 12/12) and with access to electric light presented delayed sleep onset (subjective and objective measure), shorter sleep duration (subjective measure) and delayed melatonin onset than those workers without electric light at home.

As mentioned before, older subjects show an advanced circadian phase, which cannot be explained by a shortened period of the circadian clock since, despite being observed in animal models, experimental human studies have not shown a difference between younger and older adults. In order to explain this phase advance in elderly people, mechanisms based on reduced light exposure or reduced responsiveness to light in older adults have been proposed, which could lead to age-related circadian changes.

Based on this new approach, several studies try to elucidate a possible reduction in light response in aging. The majority of experimental studies shows a reduction in responsiveness to moderate light levels, but this does not happen with high or low levels of light exposure. Also, Herljevic et al. showed that melatonin suppression in older women was less efficient compared with younger women in response to short wavelength visible light (456 nm), but no age-related change was found in melatonin suppression in response to longer wavelength light (548 nm). In other words, the ability of short wavelength light to phase shift circadian rhythms is reduced in older adults, which cannot be explained by a shortened circadian phase, and so are the main photoreceptors found in retina, a fact that could impair synchronization processes.

Despite of the well-characterized response reduction to light in elderly subjects, older subjects still responded to light in all of the mentioned studies. This fact supports the evidence and widespread use of light therapy in elderly people and its benefits. It is also known that light therapy may lead to improvement of circadian disrupts associated to some types of dementia, e.g. AD and sundowning. However, this also means that daily light exposure through technology may also exert some influence in the circadian rhythm of older subjects. Furthermore, in recent years, there was an increase in the use of light emitting electronic media, such as televisions, computers, video games and cell phones/smart phones, and several studies have evaluated the effect of exposure to these devices in the circadian system. The use of some medias at night has been associated with poor sleep quality and insomnia. However, there are contradictory studies showing that the use of electronic media can affect sleep habits (sleep onset and offset) but are not associated with sleep problems nor sleep duration.

Another way by which the use of electronic media may affect sleep patterns is through an increase in mental activity as well as through emotional and psychological issues, e.g., there is an association between the use of interactive electronic medias (computers, video games and cell phones) and complaints regarding the onset of sleep.

Comparing with what is observed in adolescents, in which the use of technologies and artificial light exposure may lead to a decrease on sleep quantity and considering that there is a major social pressure (especially referring to school schedules), the influence of light exposure may have different effects in the elderly population. Hence, if correctly used and if the light time exposure, brightness, wavelength and use of media are controlled, light exposure may have a beneficial effect on sleep, cognition and social interaction of elderly people, being capable of shifting the sleep onset and also avoiding that the phase advance which naturally occurs impairs the life quality of elderly people. This advance may result in non-conventional sleeping and awakening times, disabling the elderly subjects capacity to fulfill socials demand and leading to an impossibility of interacting with other people and in a poor life quality. Also, given that there is no consensus if diseases such as dementias appear before or after a circadian disrupt, it is not yet known if the use of light therapy associated to behavioral therapy, as the exposure to light/use of electronic medias, may avoid or delay the development of such diseases.

Since there is a limited number of studies linking the relationship between sleep-wake cycle and the effect of media use in the modern world, and there is also a lack of studies showing this connection, especially regarding the elderly population, new studies must be performed examining the
effects of using these electronic medias throughout different periods of the day. Moreover, as mentioned above, it would be of great interest trying to understand how the media use affect especially the elderly subjects, since their social needs and physiology differ largely from the main studied populations, adults and adolescents. With such knowledge, it may also allow new speculations focusing in a better approach in therapy by taking advantage of the already established use of interactive and non-interactive media by the old-age population. In conclusion, with a better understanding of the effects of light-emitting devices on the sleep patterns, better use of these devices may be implemented by the general population, but mostly by the elderly people aiming a proper use of them in a way that improves sleep and life quality in general.

GENERAL RECOMMENDATIONS

- Strengthen signaling, either by increasing light exposure throughout the light phase and reducing exposure to light in the dark phase and/or by adopting regular social commitments.
- Guiding the elderly patients so they understand that some changes of rhythmicity, such as an increased number of nighttime awakenings, are part of onto-genesis and do not necessarily reflect a disorder of circadian rhythmicity.

CONFLICT OF INTERESTS

The authors report no conflict of interests.

AUTHOR'S CONTRIBUTIONS


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